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EDITORIAL

Intrauterine Illicit Substance Exposure

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The use of illicit substances has increased dramatically over the last 10 years in Taiwan. The common drugs of abuse includes ethanol, amphetamines/methamphetamines, heroin/morphine/opiate, methadone, cocaine, marijuana, barbiturates, benzodiazepines and phencyclidine/ketamine.[1,2] The drug abusers have higher risk of unprotected sexual intercourses and subsequent pregnancies. The influence of drug abuse during pregnancy has affected women in many domains. Consequently, fetuses and infants with intrauterine exposure to illicit substances may suffer from developmental problems and withdrawal symptoms.[3–5]

Some abused substances have been reported to be potential teratogens for the fetus. In the immature mammalian brain during brain growth spurts/synaptogenesis period, the synaptic connections may be disrupted by abnormally suppressed neuronal activity and the nerve cells may receive an internal apoptosis signal as a result.[5,6] This kind of neural apoptosis can be triggered by the transient blockade of glutamate N-methyl-d-aspartate (NMDA) receptors, or the excessive activation of γ-amino-butyric acid ($GABA_A$) receptors.[7,8] The associated apoptogenic agents include anticonvulsants (barbiturates, benzodiazepines, phenytoin, valproate), anesthetics (ketamine, nitrous oxide, propofol), and some other abused substances (phencyclidine, ethanol).[6,9,10] Phencyclidine (PCP, angel dust) and ketamine (special K) are potential NMDA antagonists which induce apoptotic neurodegeneration in the developing rat brain.[7] Barbiturates and benzodiazepines are GABA mimetics that cause neuroapoptosis in the developing rodent brain.[8] Phenytoin and valproate are voltage-gated sodium ion channel blockers that may suppress neuronal activity and induce a neuroapoptotic response similar to that of the GABA mimetics in the developing rat brain.[5] Ethanol, with both NMDA antagonist and GABA mimetic properties, was found to have robust evidence of triggering a neurodegenerative response in the developing rodent brain.[11] A single ethanol intoxication episode may cause apoptosis of millions of neurons in the developing brain, with the most severely affected regions including the parietal cortex, cingulate cortex, and rostral hippocampus.[12]

Spontaneous abortion, stillbirth, fetal and infant growth retardation, fetal alcohol syndrome and attention deficit disorder have been reported to be the adverse outcomes of prenatal ethanol consumption.[13,14] The effects of intrauterine exposure of heroin/methadone include delayed physical growth, neurologic performance and cognitive development, in addition to withdrawal symptoms.[15] Decreased head circumference, hypertonia and lower cognitive scores have been described to associate with intrauterine cocaine exposure.[3,16] Smaller infants with a reduction in gestational age and small for gestational age at birth have been reported to relate to intrauterine phencyclidine/ketamine exposure.[17,18] Therefore, the fetuses, infants, or children with intrauterine substances exposure may require early intervention and follow-up treatment not only for the withdrawal symptoms, but also for the long-term sequels.[4,5]

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Among the group of women with illicit drug abuse, the number with unplanned pregnancies has increased. These groups of pregnant women seldom admit the usage of illicit substances, or usually underreport the period of usage during pregnancy. Because the maternal blood and urine drug tests are effective for recent exposure within a few days only, the maternal hair, meconium, and umbilical cord have been assessed for drug testing as means of detecting prenatal drug exposure.[19,20] In the case reported by Su et al[21] in this issue, neonatal hair and maternal hair drug tests were carried out to confirm the prenatal ketamine abuse successfully. Neonatal hair drug testing may become an alternative method for detection of intrauterine illicit drug exposure, with further investigation.

Substance dependence has become a major public health problem worldwide. Different programs of multiple substances screening for drug abusers during the parturition or prenatal care visits have been introduced in some institutes in the United States, because most pregnant abusers are unwilling to concede the usage and many drug abusers use more than one substance.[22–25] A 19% screened positive rate detected by a universal screening program has been reported at the University Hospital in New Orleans. Low birth weight and being positive for HIV were particularly prevalent in those with cocaine and/or amphetamines abuse.[25] Histories of self-reported tobacco use and ethanol use during pregnancy were found to be the indicators of illicit drug abuse.[25] In addition to the potential short-term and long-term adverse effects on children, prenatal illicit drug exposure is also associated with poor maternal nutritional status, impaired caregiving, infectious diseases and domestic violence.[26,27] Comprehensive care should be provided to the families of infants with detected prenatal illicit drug exposure. Early intervention and a better nurturing environment can improve the outcomes of these children, and the health condition of subsequent infants of the same mother.[27,28] Therefore, prenatal or neonatal illicit substance screening for high-risk cases may be helpful for both infants and their families.

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